REMARKS

The Present Invention

The present invention is directed to an adenoviral vector for expressing a heterologous gene in a host cell, a host cell infected with such a vector, a method of producing a selected protein by culturing a host cell infected with such a vector, and a method of delivering a heterologous gene to an animal heart *in vivo* by administering such a vector to the animal heart.

The Pending Claims

Claims 1, 3, 4, 9, and 17-20 are pending. Claims 1, 3, 4, 9, and 17 are directed to an adenoviral vector. Claim 18 is directed to a host cell. Claim 19 is directed to a method of producing a selected protein. Claim 20 is directed to a method of administering a heterologous gene to an animal heart *in vivo*.

The Amendments to the Claims

Claims 1 and 20 have been amended to point out more particularly and claim more distinctly the present invention. The amendments to claims 1 and 20 are supported by the instant specification at, for example, page 9, lines 11-21, page 17, line 37, through page 18, line 10, and Examples 5 and 8. Claims 21 and 22 have been cancelled in view of the amendment to claim 1. No new matter has been added by way of these claim amendments.

The Office Action

Claims 1, 9, and 17-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schneider et al., *J. Gen. Virol.*, *70*, 417-427 (1989) in view of Huang et al., *Nucl. Acid Res.*, *18*(4), 937-947 (1990), and Choi et al., *Mol. Cell. Bio.*, *11*(6), 3070-3074 (1991). Claims 3, 4, 20, 21, and 22 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of the Schneider, Huang, and Choi references in further view of Fang et al., *Hepatology*, *10*, 781-787 (1989), Kaufman et al. (U.S. Patent 4,740,461), Stratford-Perricaudet et al., *J. Clin. Invest.*, *90*, 626-630 (1992), and/or Fields (In *Fundamental Virology*, Raven Press, New York, p. 795 (1990)). Reconsideration of these rejections is hereby requested.

Discussion of Rejections Under 35 U.S.C. § 103(a)

The adenoviral vector of amended claims 1, 3, 4, 9, and 17-19 comprises at least one insertion site for cloning a selected heterologous gene in the adenoviral E1 region of the adenoviral genome. In an orientation opposite to the direction of transcription of the adenoviral E1 region, the adenoviral vector further comprises (a) a heterologous promoter positioned upstream from the insertion site, (b) a eukaryotic splice acceptor and splice donor site positioned downstream of the promoter and upstream of the insertion site, and (c) a polyadenylation sequence positioned downstream of the insertion site. The cited references, alone or in combination, do not teach or suggest the presently claimed invention.

The Schneider reference describes an adenoviral vector comprising a heterologous gene inserted into the E3 region of the adenoviral genome. The adenoviral vector comprises an intact E1 region, as evidenced by propagation of the adenoviral vector in HeLa cells (see Schneider reference at, for example, page 420, paragraph 1). There is no teaching or suggestion in the Schneider reference to modify the adenoviral vector by inserting the described expression cassette into the adenoviral E1 region. The Huang reference and Choi reference do not discuss adenovirus, but instead are directed to transgenic mice and plasmids, respectively. Likewise, the Fang reference and Kaufman reference do not describe adenoviral vectors, much less an adenoviral vector modified in the E1 region of the adenoviral genome. Accordingly, the Huang, Choi, Fang, and Kaufman references do not cure the deficiencies of the Schneider reference in rendering obvious the presently claimed adenoviral vector, and the rejection of claims 1, 3, 4, 9, and 17-19 should be withdrawn.

The method of claim 20 comprises administering to an animal heart *in vivo* an adenoviral vector that is similar to the adenoviral vector of claim 1 and contains a heterologous gene. The Office contends that one of skill in the art would have been motivated to insert the marker gene of Stratford-Perricaudet into the adenoviral vector of Schneider, Huang, and Choi because the vector of Schneider, Huang, and Choi comprises an intron which would be expected to obtain improved gene expression. However, there is no suggestion in the cited references of the adenoviral vector recited in the method of claim 20. In particular, there is no suggestion in the Schneider reference to insert the described expression cassette, which is located in the non-essential E3 region of the adenoviral genome, into the replication-essential E1 region of the adenoviral genome. Likewise, there is no suggestion in the Stratford-Perricaudet reference to modify the orientation of the expression cassette in the described adenoviral vector such that the direction of transcription of the expression cassette is opposite compared to the direction of transcription of the E1 region. The Huang and Choi references do not suggest inserting an

expression cassette into the E1 region of an adenoviral vector genome. In that the references simply do not teach or suggest the claimed invention, the rejection of claim 20 should be withdrawn.

Although the rejection of claim 21 has been rendered moot in view of the cancellation of that claim, Applicant provides the following additional comments to the extent that rejection of previously pending claim 21 is relevant to the amended claims presented herein. The Office contends that the Fields reference teaches that the adenoviral E1 and E3 regions are transcribed in the same direction, which allegedly renders obvious an adenoviral vector "in which the expression cassette is oriented oppositely to the direction of transcription of the E1 region" (Office Action dated July 16, 2003, page 7, paragraph 4). At most, the disclosure of the Fields reference constitutes a general discussion of adenoviral biology. A mere description of the direction of transcription of the E1 and E3 regions of the adenoviral genome does not constitute a teaching or suggestion to modify the adenoviral vector of the Schneider reference to position the described expression cassette in the E1 region of the adenoviral genome.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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